UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/780,566	02/12/2001	Bert Vogelstein	01107.00092	1623

22907 7590 10/18/2002

BANNER & WITCOFF
1001 G STREET N W
SUITE 1100
WASHINGTON, DC 20001

EXAMINER
YU, MISOOK

ART UNIT	PAPER NUMBER
1642	13

DATE MAILED: 10/18/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/780,566	VOGELSTEIN ET AL.	
	Examiner	Art Unit	
	MISOOK YU, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *7/29/2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The Examiner of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Misook Yu.

Claims 25-32 are pending and examined on merits.

Claim Rejections - 35 USC § 112

Rejection of claim 25 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention **is withdrawn** because applicant amended the claim.

Rejection of claims 25-32 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention **is withdrawn** because the instant invention is a screening method.

New Grounds of Rejections

Specification

The incorporation of essential material in the specification by reference to a foreign application or patent, or to a publication is improper. The specification does not teach how to measure "activity of CDK4". How to measure activity of CDK4 is essential to practice the instantly claimed invention and the incorporation of essential material in the specification by reference to a foreign application or patent, or to a publication is improper. Further, the incorporated reference does not teach how to measure CDK activity after contacting a cell with a candidate anti-tumor agent. See page 651 of Li et al (2000, Biochemistry vol. 649, pages 647-657). Further, Li et al teach a CDK4 inhibition assay using purified CDK4 in vitro, not using a cell. Applicant is required to amend the disclosure to include the material incorporated by reference. The

amendment must be accompanied by an affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application. See *In re Hawkins*, 486 F.2d 569, 179 USPQ 157 (CCPA 1973); *In re Hawkins*, 486 F.2d 579, 179 USPQ 163 (CCPA 1973); and *In re Hawkins*, 486 F.2d 577, 179 USPQ 167 (CCPA 1973).

Claim Rejections - 35 USC § 112

Claims 25-32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 25 recites "a cell which has a genetic alteration which dysregulates c-MYC expression" but it is not clear what the metes and bounds are for the phrase. The specification at page 1 lines 6-14 says that c-myc over-expression due to a genetic defect in the proto-oncogene itself or a genetic defect in upstream regulator of c-myc expression has been implicated in a variety of human tumor. However, the specification does not teach any other dysregulation for example, under-expression of c-myc is implicated in human cancers.

For the purpose of this office action, this examiner assumes that the phrase means cancer cells over-expressings c-myc. However, this treatment does not relieve applicant the burden of responding to this rejection.

Claim 25 recites "activity of CDK4" but it is not clear what the metes and bounds are for the phrase. Since the specification at the paragraph bridging pages 8 and 9 says how to measure CDK4 enzymatic kinase activity is known and refers to Li et al (cited above), this examiner will assume that the phrase means measuring CDK4 kinase activity.

Claims 25 is confusing therefore indefinite because the active steps of the claim comprises: 1) contacting a c-myc over-expressing cell with an anti-tumor candidate agent; 2) measuring CDK4 kinase activity if the agent inhibits that activity. The

specification does not teach any method directly measuring the CDK4 kinase activity. Li et al (cited above), however, does not teach how to measure the activity inside cells. Method of Li et al uses purified CDK4-cyclin D2 holoenzyme. Therefore it is not clear how the activity is measured.

Claims 25-32 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to **enable** one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claims are interpreted as drawn to method of screening an anti-tumor candidate agent using active steps comprising contacting c-myc over-expressing cells with an agent, followed by measuring CDK4 kinase activity described in Li et al (cited above). The specification does not teach how to measure the CDK4 kinase activity directly from the agent-contacted cells and Li et al teach measuring CDK4 kinase activity, (i.e. measuring transfer of phosphate from labeled ATP to GST-Rb) using purified CDK4 enzyme. Kudo et al (Clinical Cancer Research 5, pages 4279-286) describe method of screening anti-tumor candidate agents using active steps comprising lysing 60 tumor cells (from NCI drug screening panel), contacting the lysate with a candidate agent, and measuring CDK4 kinase activity by measuring transfer of labeled phosphate from ATP to GST-Rb. Note page 4280, second column under CDK Inhibition Assays. The specification does not teach any new way of measuring CDK4 kinase activity in cells and the art (see Li et al and Kudo et al) seems to teach CDK4 kinase activity is measured in vitro. Since the specification does not give any example how to screening an anti-tumor candidate agent using the active steps of claims 25-32, the status of art indicates that the measuring step involves in vitro mixing of Rb protein with source of CDK4 and labeled phosphate, not just contacting cell with a agent and directly measure CDK4 kinase activity without any further intervening step as indicated in instant claims 25-32, it is concluded that undue experimentation is necessary to figure out how to measure CDK4 activity of an anti-tumor contacted cell with dysregulated c-myc expression.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 25-32 are rejected under 35 U.S.C. 102(a) as being anticipated by Kubo et al (December 1999, Clinical Cancer Research 5, 4279-4286).

For compact prosecution of the application, claims 25-32 are interpreted as drawn to a method for screening candidate anti-cancer agents by adding a candidate agent to cell lysate of a cell over-express c-myc and measuring inhibition of CDK4 by the agent.

Kubo et al (Clinical Cancer Research 5, 4279-4286) teach a method of anti-tumor candidate agents that inhibit CDK4 kinase activity using 60 different tumor cell lines representing various tumors of NCI drug screening panel. Note page 4280. Limitations of claims 26-32 as well as the limitation in claim 25 "dysregulateion of c-MYC expression" appear to be inherent properties of the 60 NCI drug screening panel cancer cells. The Office does not have the facilities and resources to provide the factual evidence needed in order to establish that the NCI 60 different tumor cell lines the prior art used to screen agents inhibiting CDK4 kinase activity does not possess the structural and functional characteristics (dysregrulates c-myc, Burkitt's Lymphoma, neuroblastoma, colon cancer, t8:14 translocation, a genetic amplication of c-myc, a mutation in APC, a truncating mutation in APC). In the absence of evidence to the contrary, the burden is on the applicant to prove that the 60 different human cancer cell lines NCI selected for drug screening do not have characteristics, i.e. dysregrulates c-myc, Burkitt's Lymphoma, neuroblastoma, colon cancer, t8:14 translocation, a genetic amplication of c-myc, a mutation in APC, a truncating mutation in APC. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MISOOK YU, Ph.D. whose telephone number is 703-308-2454. The examiner can normally be reached on 8 A.M. to 5:30 P.M., every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony C Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Misook Yu
October 16, 2002

MARY E. MOSHER
PRIMARY EXAMINER
GROUP 1800 1600